

Osteoarthritis and Cartilage



Trends in incidence and prevalence of osteoarthritis in the United Kingdom: findings from the Clinical Practice Research Datalink (CPRD)



S. Swain [†]#, A. Sarmanova [‡], C. Mallen [§], C.F. Kuo ^{||}, C. Coupland [¶], M. Doherty [†]#, W. Zhang [†]#*

[†] Academic Rheumatology, Division of Rheumatology, Orthopaedics and Dermatology, University of Nottingham, UK

[‡] Bristol Medical School, Population Health Sciences, University of Bristol, UK

[§] School of Primary, Community and Social Care, Keele University, UK

^{||} Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, 5, Fu-Hsing Street, Taoyuan, 333, Taiwan

[¶] Division of Primary Care, School of Medicine, University of Nottingham, UK

Versus Arthritis Pain Centre, University of Nottingham, UK

ARTICLE INFO

Article history:

Received 26 September 2019

Accepted 5 March 2020

Keywords:

Osteoarthritis

Trends

UK

Burden

Incidence

Prevalence

SUMMARY

Objective: This study aimed to explore the incidence and prevalence of OA in the UK in 2017 and their trends from 1997 to 2017 using a large nationally representative primary care database.

Design: The UK Clinical Practice Research Datalink (CPRD) comprising data on nearly 17.5 million patients was used for the study. The incidence and prevalence of general practitioner diagnosed OA over a 20 years period (1997–2017) were estimated and age-sex and length of data contribution standardized using the 2017 CPRD population structure. Cohort effects were examined through Age-period-cohort analysis.

Results: During 1997–2017, there were 494,716 incident OA cases aged ≥ 20 years. The standardised incidence of any OA in 2017 was 6.8 per 1000 person-years (95% CI 6.7 to 6.9) and prevalence was 10.7% (95% CI 10.7–10.8%). Both incidence and prevalence were higher in women than men. The incidence of any-OA decreased gradually in the past 20 years at an annual rate of -1.6% (95%CI -2.0 to -1.1%), and the reduction speeded up for people born after 1960. The prevalence of any-OA increased gradually at an annual rate of 1.4% (95% CI 1.3 – 1.6%). Although the prevalence was highest in Scotland and Northern Ireland, incidence was highest in the East Midlands. Both incidence and prevalence reported highest in the knee followed by hip, wrist/hand and ankle/foot.

Conclusion: In the UK approximately one in 10 adults have symptomatic clinically diagnosed OA, the knee being the commonest. While prevalence has increased and become static after 2008, incidence is slowly declining. Further research is required to understand these changes.

© 2020 The Authors. Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International.

This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Introduction

Osteoarthritis (OA) is one of the commonest long-term conditions, causing significant impairment of physical function. It can affect several joints which may further compound functional impairment and participation restriction. In the absence of any cure, the burden of OA is increasing globally with an estimated 28% of the older population (>60 years) having OA¹. The 2017 Global Burden of Disease (GBD) report ranked hip and knee OA as the 11th

highest contributor to global disability and the 23rd highest cause of disability adjusted life years (DALYs)². Increasing life expectancy and the ageing population are expected to make OA the fourth leading cause of disability by 2020³ and a significant increase in DALYs has already been noted from 2007 to 2017.²

Whilst DALYs provide useful data on disease burden, accurate information on changing incidence and prevalence of a disease provides an alternative picture to help guide effective preventive and management planning. To date, very few studies have examined trends of OA incidence and prevalence using national representative cohort data. The lack of such information creates challenges in reliable estimation of the burden of OA. Worldwide, the estimated incidence of OA has varied from a low of 14.6 per

* Address correspondence and reprint requests to: W. Zhang, Academic Rheumatology, Clinical Sciences Building, City Hospital, Nottingham, NG5 1PB, UK.

E-mail address: weiya.zhang@nottingham.ac.uk (W. Zhang).

1000 person-years in Canada⁴ to a high of 40.5 per 1000 person-years in the UK⁵. Only three countries have reported increasing trends of the incidence of OA, whereas none has published prevalence trend data. In Sweden, age-standardized hospitalization rates due to hip and knee OA increased from 1998 to 2014⁶ and in Canada crude incidence rates increased during 2000–2008 from 11.8 to 14.2 per 1000 person-years in men, and from 15.7 to 18.5 person-years in women⁴. However, one UK study using the Clinical Practice Research Datalink (CPRD) reported no change in trends of incidence of physician-diagnosed OA (1992–2013)⁵. Seven years of consultation data till 2010 reveals nearly 8.75 million people in the UK had visited any health facility for treatment of OA, and by 2035, 8.3 million people in the UK aged 45 years or over could have symptomatic knee OA.⁷

Primary care is the usual first point of contact for someone with symptomatic OA. The UK CPRD is a primary care database that represents the community burden in better ways than hospital (secondary care) records and allows evaluation of the trends of incidence and prevalence over time. However, these estimates depend on the nature of consultation, the coding system and other individual factors. While the incidence measures the aetiological impact of OA, the prevalence measures the disease burden to inform health resource requirements. Although there have been some incidence and prevalence studies from the UK^{5,8,9}, they have given inconsistent results through use of different definitions and sampling methods. Therefore, the recent trend and natural history of OA in UK primary care remains largely unknown.

This study aimed to explore both the incidence and prevalence of OA (overall and joint specific) in the UK during the period 2017 and their trends during 1997–2017 using a large nationally representative primary care database.

Methods

This was a descriptive study using longitudinal primary care database of the UK.

Source population

The CPRD is a large database of general practice electronic medical records that is generalisable to the wider UK population. As of 31st December 2017, the CPRD contained data on 17,480,766 individuals from 736 general practices. Recording of ailment is mandatory for every visit and there is no limit on the number of diagnoses entered. The database contains information on symptoms, diagnoses, prescriptions, referrals, tests, immunisations, life style factors, information on medical staff, health promotion activities, management and quality outcome framework indicators¹⁰. Substantial research has been undertaken to examine the validity and completeness of the CPRD and has provided satisfactory results¹¹. More details about the database can be found at <https://cprd.com/primary-care>. This study was approved by the independent scientific advisory committee for CPRD research (protocol reference: 19_030 R). No further ethical permissions were required for the analyses of these anonymized patient level data.

Study population

CPRD data available for patients registered from 1st January 1997 until 31st December 2017 was used for the study. Inclusion criteria were individual records with: (1) people aged 20 years or more during each study year of 1997–2017; (2) active registration for at least 12 months with the up-to-standard practice prior to the study start date (determined by CPRD database standards); and (3) data quality flagged as ‘acceptable’ in the database.

Case definition of OA

Incident OA was defined as the first diagnosis of OA within each study year. Prevalent OA was defined as having an OA diagnosis by 1st July of each study year. We used Read codes: a medical coding system of clinical terms used by national health services (NHS), UK¹². The available Read code list (www.keele.ac.uk/mrr) to identify people with a General Practitioners (GP) diagnosed OA was adapted according to our inclusion and exclusion criteria. We used the exact list but excluded two OAs (acromio-clavicular and sterno-clavicular joints), because of the possible low accuracy of diagnosis at these joints and the expected incidence is very low. The codes obtained from the given website was previously matched with ICD-10 codes (Musculoskeletal disorder chapter)⁹. Even though not all OA joint codes have been validated, a recently published article shows the positive predictive value (PPV) for Read codes for hip OA in people aged 60 and over was nearly 80% and suitable for research purposes¹³. The Read codes for OA (N05...) used in the study was further screened by two independent GPs before the use (Appendix 1).

The index date was defined as the date of the first diagnosis of OA recorded in the database. Patients meeting the following criteria were excluded from both incidence and prevalence estimation: (1) any recording of joint diseases (rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, ankylosing spondylitis, septic arthritis, spondyloarthropathy or crystal disease and human parvovirus B19 infection) before or within 3 years after the index date; (2) any record of specific non-OA diagnosis (soft-tissue disorders, other bone/cartilage diseases) at the same joint in the 12 months before or after the recorded OA consultation; and (3) any history of joint injury within 1 year prior to the index date. In the absence of a recording of OA during the study year, any recording of joint replacement was taken as a proxy measure of OA.

Estimation of incidence and prevalence

The annual incidence rate for OA was defined as the number of incident (new) OA cases between 1st January and 31st December, divided by the number of person-years at risk for each calendar year from 1997 to 2017. Person-years of follow-up were calculated for eligible people at risk (i.e., no previous diagnosis of OA) from the latest of 1st January to the earliest date of transfer-out, last data collection, incident diagnosis of OA, death or 31st December of the study year. The annual prevalence of OA was calculated by dividing the number of people ever diagnosed with OA at 1st July of each calendar year, by the total number of eligible people in the population at the same time point of the calendar year.

Statistical analysis

The incidence and prevalence for each year from 1997 to 2017 were standardised according to age (5 years band), sex and length of data contribution (observation period) using the CPRD population structure in the year 2017 as reference. This method of adjustment for the observation period has been used previously¹⁴. The length of data contribution of each patient was defined as the period from the up to standard date for participants to 1st July of each calendar year for prevalence and 1st January of each calendar year for incidence. Up to standard date is always later the registration date. The length of data contribution was then categorised in four groups 0–3 years, 4–6 years, 7–9 years and ≥ 10 years. Standardization by length of data contribution was done because higher estimates were observed for longer lengths of data contribution (Supplementary fig S1). For 1997, no data contribution was seen for ≥ 10 years (Supplementary Figs. S1 and S2). Because, even

though the first registration date with the database was traced back before 1987, the up to standard practice data started recording in 1988, which is acceptable as a quality data, as per CPRD. For sex specific estimation, only age and length of data contribution standardisation was done. Age-sex standardized incidence and prevalence of OA in 2014 were calculated for all 13 regions of the UK and plotted using choropleth maps in QGIS software (V.3, Open source)¹⁵. The prevalence and incidence for the UK region after 2014 could not be estimated adequately because of lack of information from the East Midlands region from 2015 onwards.

Age-sex and length of data standardized trends (overall and sex specific) of the incidence and prevalence of OA were calculated for any-OA, joint specific and unspecified OA for 1998–2017. Unspecified OA cases are coded as 'unspecified' in the database without any mentioning of the site involved. We computed the incidence and prevalence across each age group for both sexes only for the year 2017. The 95% confidence interval (CIs) were derived based on the assumption of a Poisson distribution for the observed cases. The trends were tested using Joinpoint regression analysis¹⁶ with Joinpoint software (Version 4.6.0.0)¹⁷. Bayesian Information Criterion (BIC) was used to identify the 'join points', which describes the significant change across the trend line and best-fit data series. Using BIC, a maximum of three joinpoints were selected. Annual percentage changes (AAPC) for each segment and average AAPC for the entire study period were calculated at the significance level of 0.05 using the empirical model¹⁸. Additional, trend analysis of joint pain incidence was done using the same database. Details are provided in [Supplementary Fig. S8](#).

Both incidence and prevalence trends were modelled as a function of age at diagnosis, period (year of diagnosis) and birth (year of birth) cohort. To assess the cohort effect, age-period-cohort (A-P-C) analysis was undertaken¹⁹. For visual clarity incidence and prevalence were aggregated in 5-year age groups for period and birth cohort graphs. The A-P-C analysis was performed in R using the package 'Epi' and 'APC'^{20–22}. Statistical analyses were

performed using STATA (SE v 15, STATA corp, Texas) and R(V 5.2, R software, Austria).^{23,24}

Results

Incidence and prevalence

In 2017, the total person-years of follow up for any-OA was 1,495,497 with 10,147 incident OA cases, and the incidence was 6.8 per 1000 person-years (95% CI 6.7 to 6.9 per 1000 person-years). The incidence was higher in women (8.1; 95% CI 7.9 to 8.3) than in men (5.5; 95% CI 5.3 to 5.7 per 1000 person-years). The age-specific incidence in 2017 shows that OA was very rare in people less than 30 years of age. The incidence was 0.08 per 1000 person-years in both sexes which increased gradually with age and peaked at 75–79 years at 27 per 1000 person-years (95% CI 23.5 to 29.8 per 1000 person-years) in women and 18 per 1000 person-years (95% CI 15.4 to 20.6 per 1000 person-years) in men [Fig. 1(A)].

Of 1,690,618 eligible individuals in 2017, 181,464 had a recorded diagnosis of any-OA. The prevalence in 2017 was 10.8% (95% CI: 10.7–10.9%) which was higher in women (12.8%; 95% CI 12.8–12.9%) than men (8.6%; 95% CI 8.5–8.7%) across all age groups. The prevalence increased sharply at age 40–44 years in women and 45–49 years in men. In both men and women, the increasing trend continued until age group of >80 years, reaching the peak of 47% for women and 35% for men [Fig. 1(B)].

The joint-specific OA incidence (per 1000 person-years) in 2017 was highest for knee (2.3; 95% CI 2.2 to 2.4) followed by hip (1.1; 95% CI 1.1 to 1.2), wrist and hand (0.65; 95% CI 0.6 to 0.7) and ankle and foot (0.2; 95% CI 0.2 to 0.2). The incidence of unspecified OA was 5.2 per 1000 person-years (95% CI 5.1 to 5.3). All joint-specific incidence rates were higher in women than in men. The detailed distribution across age in both men and women is given in [Supplementary Fig. S3](#). In descending order, the overall prevalence according to joint site in 2017 was; knee (2.9%, 95% CI 2.7–2.9%), hip (1.5%, 95% CI 1.4–1.5%), wrist or hand (0.5%, 95% CI 0.5–0.5%) and

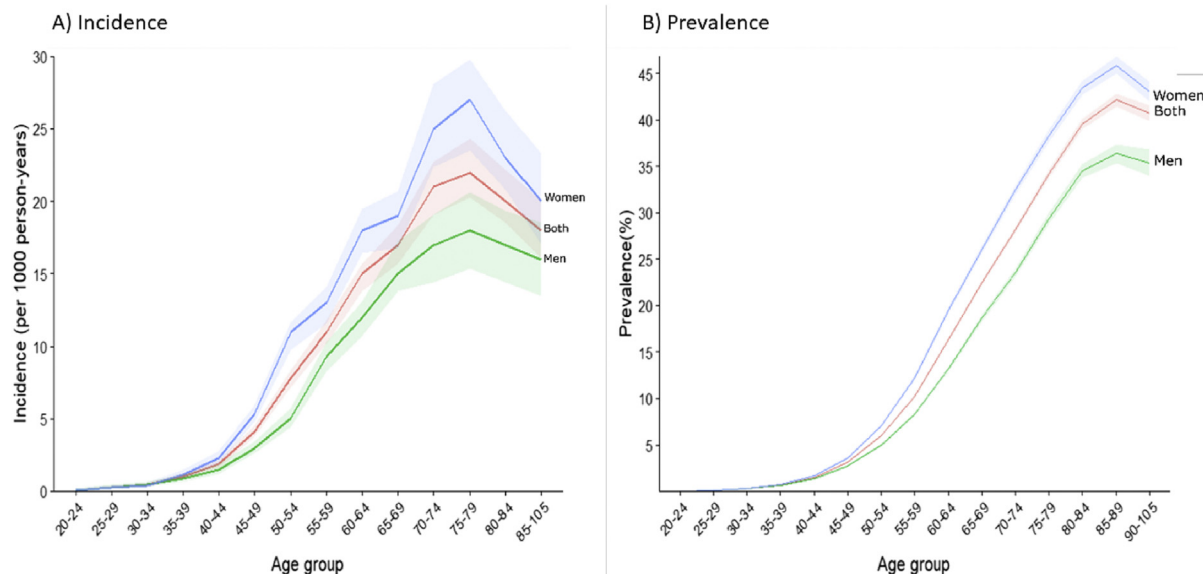


Fig. 1 Age specific incidence (A) and prevalence (B) of OA in 2017.

| Year | Incidence (per 1000 person-years) | | | | | Prevalence (%) | | | | |
|----------|-----------------------------------|---------|--------------------------|-------------------------------|-----------------------------------|---------------------|---------|---------------------------|-------------------------------|-----------------------------------|
| | Person-Year | Cases | Crude Incidence [95% CI] | Age-sex standardized [95% CI] | Age-sex-LOD standardized [95% CI] | Eligible population | Cases | Crude Prevalence [95% CI] | Age-sex standardized [95% CI] | Age-sex-LOD standardized [95% CI] |
| 1997 | 1,321,487 | 12,296 | 9.30 [9.14–9.47] | 9.17 [9.00–9.34] | | 5,711,501 | 195,362 | 3.42 [3.40–3.44] | 6.15 [6.11–6.19] | |
| 1998 | 1,509,159 | 14,817 | 9.81 [9.66–9.97] | 9.05 [8.89–9.20] | 9.50 [7.43–12.67] | 5,781,677 | 215,113 | 3.72 [3.70–3.74] | 7.20 [7.16–7.24] | 8.23 [8.06–8.40] |
| 1999 | 1,831,971 | 17,216 | 9.39 [9.26–9.54] | 8.87 [8.73–9.01] | 9.69 [9.00–10.37] | 5,848,216 | 234,835 | 4.01 [3.98–4.03] | 7.41 [7.37–7.45] | 8.47 [8.39–8.55] |
| 2000 | 2,262,732 | 20,599 | 9.10 [8.98–9.22] | 8.97 [8.84–9.11] | 9.61 [9.31–9.92] | 5,896,329 | 255,264 | 4.32 [4.30–4.35] | 7.41 [7.37–7.44] | 8.94 [8.88–9.00] |
| 2001 | 2,534,401 | 23,615 | 9.31 [9.19–9.43] | 9.20 [9.07–9.32] | 9.36 [9.15–9.57] | 5,900,383 | 276,091 | 4.77 [4.74–4.80] | 7.87 [7.83–7.90] | 9.08 [9.03–9.13] |
| 2002 | 2,858,237 | 26,597 | 9.30 [9.19–9.41] | 9.37 [9.25–9.49] | 9.64 [9.44–9.84] | 5,862,771 | 296,445 | 5.05 [5.02–5.08] | 7.98 [7.95–8.01] | 9.27 [9.22–9.32] |
| 2003 | 3,046,692 | 29,358 | 9.63 [9.52–9.74] | 9.63 [9.51–9.74] | 10.00 [9.81–10.19] | 5,788,957 | 317,611 | 5.48 [5.45–5.51] | 8.19 [8.16–8.22] | 9.47 [9.42–9.52] |
| 2004 | 3,247,175 | 32,543 | 10.02 [9.91–10.13] | 10.06 [9.95–10.17] | 10.42 [10.23–10.61] | 5,705,620 | 339,718 | 5.95 [5.92–5.98] | 8.55 [8.52–8.58] | 9.77 [9.73–9.82] |
| 2005 | 3,317,484 | 33,093 | 9.97 [9.86–10.08] | 10.15 [10.04–10.26] | 10.33 [10.15–10.52] | 5,615,033 | 363,534 | 6.47 [6.43–6.52] | 9.06 [9.03–9.09] | 10.21 [10.16–10.26] |
| 2006 | 3,346,598 | 30,840 | 9.21 [9.11–9.31] | 9.39 [9.29–9.50] | 9.55 [9.37–9.72] | 5,467,107 | 378,799 | 6.92 [6.90–6.94] | 9.44 [9.42–9.47] | 10.62 [10.57–10.66] |
| 2007 | 3,374,993 | 30,236 | 8.95 [8.88–9.06] | 9.15 [9.04–9.25] | 9.49 [9.32–9.65] | 5,294,313 | 388,708 | 7.34 [7.30–7.38] | 9.73 [9.71–9.76] | 10.64 [10.60–10.68] |
| 2008 | 3,381,824 | 30,261 | 8.94 [8.84–9.05] | 9.20 [9.10–9.30] | 9.59 [9.44–9.74] | 5,112,496 | 398,003 | 7.78 [7.74–7.82] | 10.07 [10.04–10.10] | 10.91 [10.87–10.95] |
| 2009 | 3,362,701 | 29,387 | 8.73 [8.63–8.83] | 8.99 [8.89–9.10] | 9.36 [9.22–9.50] | 4,924,529 | 405,402 | 8.23 [8.20–8.26] | 10.35 [10.32–10.38] | 10.91 [10.88–10.95] |
| 2010 | 3,314,620 | 27,133 | 8.18 [8.09–8.28] | 8.42 [8.32–8.52] | 8.74 [8.62–8.87] | 4,689,058 | 403,343 | 8.60 [8.56–8.64] | 10.54 [10.51–10.57] | 10.93 [10.90–10.96] |
| 2011 | 3,235,505 | 26,100 | 8.06 [7.96–8.16] | 8.30 [8.20–8.40] | 8.48 [8.36–8.59] | 4,421,201 | 398,434 | 9.01 [8.96–9.06] | 10.69 [10.66–10.72] | 10.94 [10.91–10.97] |
| 2012 | 3,196,392 | 24,727 | 7.73 [7.64–7.83] | 7.95 [7.85–8.05] | 8.10 [7.90–8.30] | 4,165,371 | 391,691 | 9.40 [9.36–9.44] | 10.76 [10.73–10.79] | 10.87 [10.84–10.90] |
| 2013 | 3,030,317 | 23,409 | 7.72 [7.62–7.82] | 7.87 [7.77–7.97] | 7.94 [7.84–8.05] | 3,812,788 | 374,298 | 9.82 [9.78–9.86] | 10.87 [10.84–10.90] | 10.90 [10.87–10.93] |
| 2014 | 2,758,065 | 21,113 | 7.65 [7.55–7.75] | 7.74 [7.64–7.85] | 7.75 [7.65–7.86] | 3,314,992 | 337,168 | 10.17 [10.14–10.20] | 10.96 [10.93–10.99] | 10.95 [10.92–10.98] |
| 2015 | 2,360,852 | 17,690 | 7.49 [7.38–7.60] | 7.52 [7.41–7.63] | 7.51 [7.40–7.62] | 2,761,702 | 290,020 | 10.50 [10.47–10.53] | 10.94 [10.90–10.97] | 10.93 [10.90–10.96] |
| 2016 | 1,889,587 | 13,540 | 7.16 [7.04–7.28] | 7.18 [7.06–7.30] | 7.17 [7.05–7.29] | 2,100,061 | 223,948 | 10.66 [10.63–10.69] | 10.96 [10.93–11.00] | 10.95 [10.92–10.99] |
| 2017 | 1,495,497 | 10,146 | 6.78 [6.67–6.93] | 6.78 [6.67–6.93] | 6.78 [6.67–6.93] | 1,690,618 | 181,464 | 10.77 [10.72–10.82] | 10.77 [10.72–10.82] | 10.77 [10.72–10.82] |
| AAPC (%) | | 494,716 | | | –1.6[–2.0 to –1.1] | | | | | 1.4 [1.3 to 1.6]* |

Age-sex and length of data contribution (LOD) standardization was done using 2017 CPRD population as standard population. For 1997, LOD standardisation was not calculated because of absence of data for ≥ 10 years (See [Supplementary Figs. S1 and S2](#)).

IR: Incidence Rate; CI: Confidence Interval; AAPC: Annual Average Percentage Change; *P-value.

Table 1 Crude and standardized incidence and prevalence of OA in the UK from 1997 to 2017

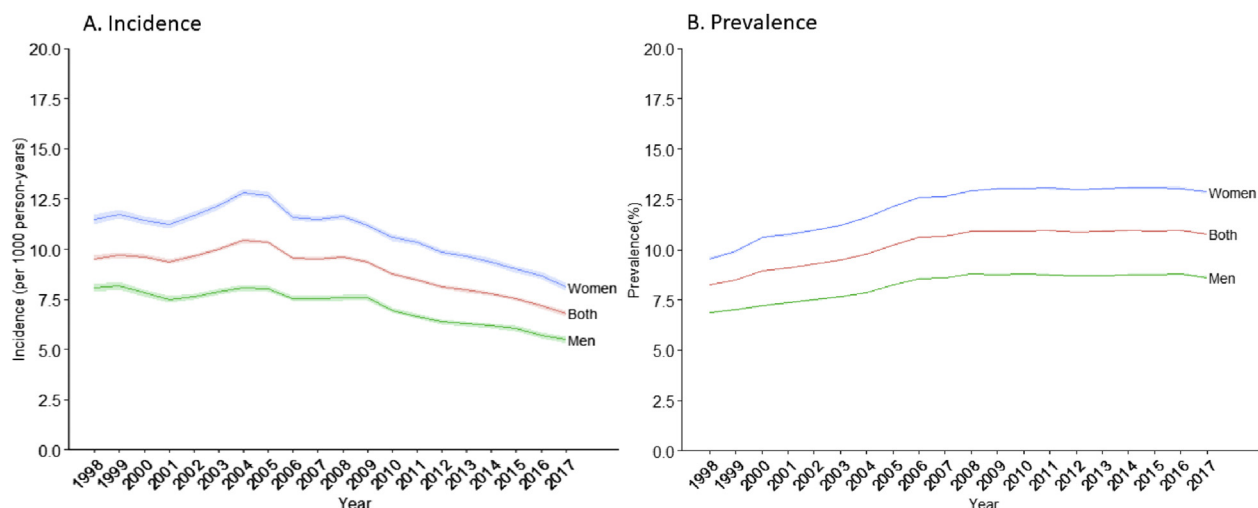


Fig. 2 Trends of standardized incidence (A) and prevalence (B) between 1998 and 2017.

Osteoarthritis
and Cartilage

ankle or foot (0.3%, 95% CI 0.3–0.3%). The prevalence of unspecified OA was 7.6% (95% CI 7.5–7.6%). The distribution of joint site and unspecified OA across the sex is provided in [Supplementary Fig. S4](#).

Temporal trends of incidence and prevalence

The incidence (both crude and standardised) of any OA decreased over time during the study period, changing from 9.5 per 1000 person-years (95% CI 9.4 to 9.7 per 1000 person-years) to 6.8 per 1000 person-years (95% CI 6.7 to 6.9 per 1000 person-years) ([Table 1](#)). Similar trends were seen in both women and men [[Fig. 2\(A\)](#)]. The incidence of OA in men declined from 8.0 per 1000 person-years (95% CI 7.8 to 8.3 per 1000 person-years) in 1997 to 5.5 per 1000 person-years (95% CI 5.3 to 5.7 per 1000 person-years) in 2017, whereas in women the incidence reduced from 11.5 per

1000 person-years (95% CI 11.2 to 11.7 per 1000 person-years) to 8.1 per 1000 person-years (95% CI 7.9 to 8.3 per 1000 person-years). Joinpoint analysis identified two points of changes in overall trend at 2002 and 2005. The AAPC was -1.6% (95% CI -2.0 to -1.1%), indicating a slight decline in the incidence since 1998. Women (-1.91% ; 95% CI -2.2 to -1.6%) had a higher decline in rates compared to men (-1.5% ; -1.1 to -1.9%). No change in trend was observed for ankle and foot and wrist and hand sites. Whereas, unspecified OA trend was on decline, while OA at knee and hip showed slightly increasing trend. Details of joint specific incidence trends are given in [Supplementary Fig. S5](#) and sex wise distribution is given in [supplementary table S1](#).

In contrast, prevalence increased from 1998 to 2017 ([Table 1](#)). The age and length of data standardised rates were found to rise in both men and women across the years. The overall prevalence of

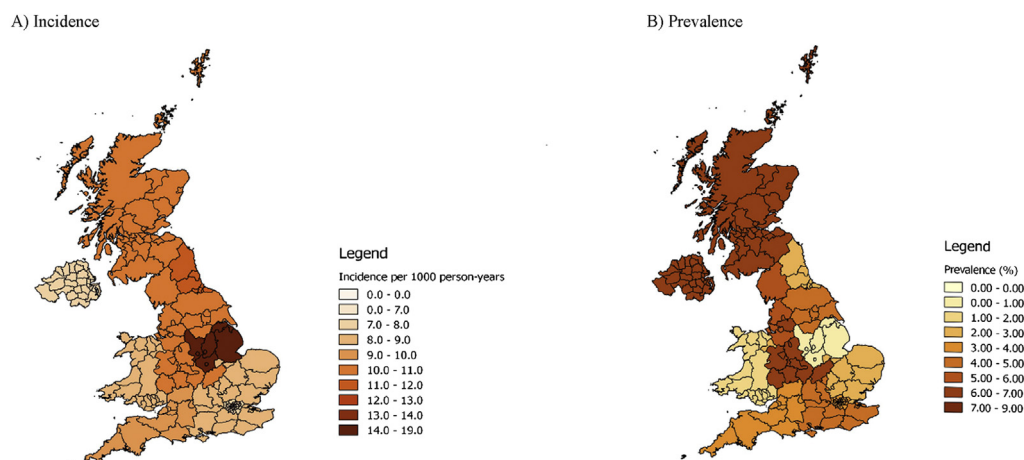


Fig. 3 Geographic variations in the incidence (A) and prevalence (B) of OA in the UK in 2014.

Osteoarthritis
and Cartilage

people with any OA in 2017 was found to increase to 10.7% from 8.2% in 1998, 1.3 times increase in prevalence over this period [Fig. 2(B)]. The average annual percentage change was 1.4% (95% CI 1.3–1.6%) for any OA, whereas among women it was a 1.6% (95% CI 1.4–1.8%) and in men a 1.3% (95% CI 1.1–1.4%) change each year. The prevalence of OA in joint-specific OA in 2017 also increased from 1998 except for ankle and foot. Details are given in [Supplementary Fig. S6](#) and sex wise distribution is given in [supplementary table S2](#). The additional analysis on trends of incidence of joint pain recorded in the CPRD shows a sudden increase in the trends after 2003 ([Supplementary Fig. S8](#)).

Geographic distribution

In 2014, the East Midlands and the North East had the highest incidence rates of OA of 12.6 per 1000 person-years and 11.7 per 1000 person-years respectively. Lowest incidence rates were seen in Northern Ireland and South East England [Fig. 3(A)]. The prevalence of any OA varied from one region to another within the UK. In 2014 the highest age and sex standardised prevalence were in Scotland, West Midlands and Northern Ireland ranging from 7% to 9%. The prevalence ranged from 3% to 5% in the Southern region [Fig. 3(B)].

Cohort effects

The incidence was found to decline according to the birth cohorts. For people in the same age group, those born later were less likely to have OA than those born earlier (Fig. 4). The reduction speeded up gradually after 1960, particularly for people aged 20–40 years, suggesting a potential aetiological change after 1960 that led to people being less likely to develop OA. In contrast, prevalence increased gradually by age but remained almost constant for people born after 1960. The plot of distribution of incidence and prevalence across the age groups for different periods of birth is provided as supplementary material ([Supplementary Figs. S7\(A\) & S7\(B\)](#)).

Discussion

This study confirms a high burden of OA in the UK with a current (year 2017) prevalence of 10.7% and incidence of 6.8 per 1000 person-years in people aged 20 and over. The prevalence of OA has increased at a rate of 1.4% per year since 1998, whereas the incidence is declining at a rate of –1.6% per year. Geographically, the prevalence and incidence of OA are not uniformly distributed. Scotland, Northern Ireland and West Midlands had higher prevalence compared to the rest of the country, whereas, the incidence was higher in East midlands and North-Eastern regions.

The standardised incidence of OA in 2013 estimated from CPRD among people aged 45 years or more was 6.3 per 1000 person-years⁵. In another study, Yu *et al.* reported the standardised rates of any OA incidence in 2010 as 8.6 per 1000 person-years among persons aged 15 years or more in a UK regional administrative database²⁵. According to the literature, the prevalence of OA among people aged 45 years and over varies between 20% and 35%^{26,27}. Our estimated prevalence among people aged 45 years or more using the entire CPRD database was nearly 23%. Global burden of disease reports the prevalence of knee and hip was 7.3% and musculoskeletal disease profile report from the NHS shows the prevalence in 2015–16 was nearly 12%^{2,28}. Comparing the incidence and prevalence across studies is very difficult because of the wide differences in study population, case definition, database quality and standardisation methods^{4,27,29}. Values similar to our prevalence estimates have been reported in the UK by Jordan *et al.*³⁰ using a database with better recording pattern, as the GPs from this region actively participate in musculoskeletal research.³¹

These differences should not affect comparisons within the study such as, incidence by age and sex. The increase in incidence and prevalence of OA with age and in women supports existing epidemiological evidence³². The sudden rise of both prevalence and incidence at age of 40 years in women has been explained through biological sex hormone changes and also has been reported uniformly in previous studies^{33,34}. The incidence pattern with age also concurs with previous studies in the UK and other countries.^{5,29}

In both sexes, the prevalence and incidence of 'unspecified' OA was high compared to reported joint-specific OA, a finding also reported by Yu *et al.*²⁵ Such 'unspecified' reporting reflects the

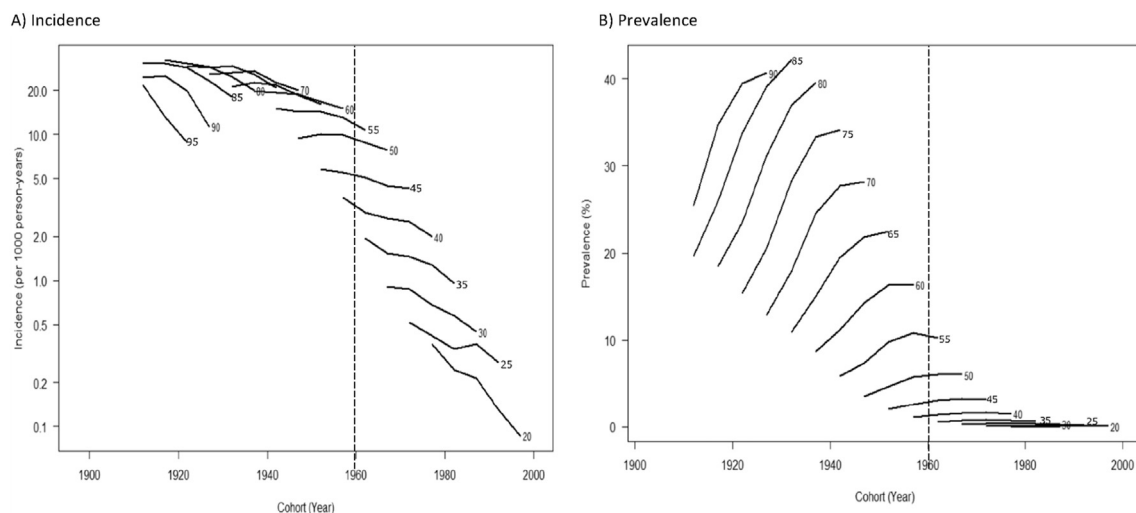


Fig. 4

Age-period-cohort analysis of trend of OA (1997–2017) incidence (A) and prevalence (B) in the UK.

recording pattern in primary care, though whether the term ‘unspecified’ is a substitute to record multiple joint involvement, remains unclear. The higher burden of knee and hip OA in this study reflects consultation behaviour, for example a preference to seek advice for large joint rather than small joint problems. There is wide variation in reported prevalence of OA at individual joint sites. Again, this could indicate different methods of ascertainment, and whether diagnosis is purely clinical or based on presence of radiographic OA changes. Also the findings are likely to under-represent true prevalence and incidence, as more than 12% of people with hip OA never consult GPs about their condition, even if it is symptomatic.¹³

Trends of incidence and prevalence

Surprisingly, there was an overall slow decline in incidence rates for any-OA since 1998. Yu *et al.* found no change in trends of incidence physician-diagnosed OA for the period 1997–2013 among people aged 45 years or more⁵. One other population-based study in the US found no increase in trends of radiographic knee OA during the period 1974–1994 after adjusting for body mass index (BMI) change³⁵. The Joinpoint analysis reveals a slight rise in incidence from 2000 to 2004 followed by a slow decline. We found significant increase in rate for knee and hip joint-specific incidence, but the ‘unspecified’ OA rate was declining, indicating possible improvement in clinical coding. Perhaps the increase in trend of ‘joint-pain’ after the year 2005 partially explains the gap (Supplementary Fig. S6) if physicians became more prone to report symptoms rather than a specific diagnosis. We observed a nearly 1.3 times increase in standardized prevalence of OA from 1998 to 2017, with an annual percentage increase of 1.4%. Globally, contribution of OA to the total prevalent cases has increased by 8.5% from 1990 to 2017 and in the UK the prevalence has increased from 6.3% in 1990–7.7% in 2017². The increase in prevalence with the slow declining incidence rate is surprising. Especially, the increased prevalence trend could be because of the cumulative nature of the longitudinal database from electronic health records. CPRD is a dynamic database with people moving in and out of the database at any time point, which changes the eligible population every year. Also, we found the prevalence trend is becoming stable since 2008, which partially explains the effect of declining incidence.

Age-period-cohort effects, length of data contribution and the participation of practices in the CPRD database influence the incidence estimates^{14,30}. Our age-period-cohort analysis shows a strong cohort effect in incidence among people born after the 1960s. It suggests that people born after this period may expose less to physically very demanding occupations such as coal-mining, farming and certain heavy industrial work because of change in patterns of occupation in the UK since 1960s including the mining activities³⁶. We standardised for the length of data contribution period to eliminate the problem of prevalent cases for OA for robust incidence estimates. In contrast, prevalence remained almost unchanged in people born after 1960s (Fig. 4), indicating the treatment of this condition may remain same.

Geographical distribution

Scotland and the middle region of England had higher incidence rates in 2014 compared to the rest of the UK⁵. The reasons for regional variation could be differences in practice areas, socio-economic conditions, lifestyles and health seeking behaviours. Interestingly, higher prevalence in the Northern region largely

matches the obesity distribution in the Northern region of the UK compared to the South.³⁷

Limitations of the study

In addition to the highlighted caveats on coding of the diseases and data contribution, a few more limitations do exist. The case definition relied on the clinical diagnosis by the general practitioners without requiring demonstration of structural OA on imaging. However, concordance between symptoms and radiographic OA (the usual way to assess structural OA) is variable and often poor, depending on the joint site being assessed³⁸. Patient-centred outcomes rather than imaging changes are key determinants of disability and burden of disease, and the National Institute for Health and Care Excellence (NICE) recommends that a purely clinical diagnosis is sufficient and that imaging should be reserved for specific situations such as atypical clinical features or rapid progression of symptoms³⁹. Coding of joint specific OA in a consultation database is always controversial. The index date reflects the date of allocation of Read codes for OA and does not reflect disease onset or the date of diagnosis. However, the date of allocation of a Read code for OA would be expected to be within a few months of the date of diagnosis¹³. We did not perform a validation study for the OA definitions used in this study, therefore the results are open to misclassification bias. Caution must be taken when comparing the prevalence and incidence of this study with that reported in other studies. However, we believe this will not affect the internal validity, such as prevalence and incidence by age and gender, and temporal trends of OA/joint pain in the past 20 years in the UK as they all were based on the same Read codes to define the disease. Furthermore, because our estimates are based on GP consultations for symptomatic regional joint pain, and not all people with symptomatic OA will consult their GP, these data may underestimate the true community prevalence and incidence of symptomatic OA. Unlike other chronic conditions, OA is not included in Quality and Outcome Framework (QOF) by the NHS in 2004. QOF is an incentivising program, which rewards GP practices in England for quality delivery of primary care including the diagnosis and recording of conditions. Therefore, the prevalence and incidence might have been underestimated. In addition, the exclusion criteria used in our study might have led to underestimation of the burden. Also, health care accessibility might influence the estimation. CPRD might have the duplication of people, because of the movement of patients from one practice area to other and being recorded with new unique identifier. However, we assume, the rate of migration might be similar in both OA group and ‘at-risk’ population. Even though, the method of standardising by length of data observation has been used previously for calculating trends using electronic health records, some residual confounding by length of data observation might still exist. Another limitation is the geographical presentation of the estimates, which needs cautious interpretation because of the non-uniform practices involved in the database.

Conclusion

One in 10 adults aged 20 years or more in the UK has GP-diagnosed OA and the knee was the leading site. The incidence of GP-diagnosed OA is declining, but the prevalence is rising slowly in the UK. A cohort effect was observed, that is, within the same age groups people born after 1960s had lower incidence than those born earlier. If it is a real change in trend or change in recoding and

reporting pattern needs to be studied. Also, further research is necessary to understand these temporal trends in OA.

Contributor and guarantor information

SS, WZ and MD conceived and designed the study. SS and WZ acquired the data. SS performed the analysis and CC, AS and WZ supervised the statistical analysis. SS, AS, CM, CC, WZ, CFK and MD interpreted the results. SS and WZ drafted the manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. WZ, CC and MD supervised the study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Competing interests

This study had no financial competing interests.

The authors declare that they have no conflict of interest.

Funding

This work was supported by Versus Arthritis [grant numbers 20777, 21595] formerly Arthritis Research UK; The University of Nottingham Vice-Chancellor Scholarship and Beijing Joint Care Foundation Scholarship. CM is funded by National Institute for Health Research (NIHR)- Research Professorship (NIHR-RP-2014-04-026), the NIHR Collaborations for Leadership in Applied Health Research and Care West Midlands and the NIHR School for Primary Care Research. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Role of the funding sources

The sponsors did not participate in the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript and the decision to submit the manuscript for publication.

Studies involving humans or animals

No direct participant recruitment was done for the study. This study was approved by the independent scientific advisory committee for CPRD research (protocol reference: 19_030 R).

Acknowledgements

We would like to thank the University of Nottingham, UK and Beijing Joint Care Foundation, China for financially supporting the research. The authors would like to acknowledge Keele University's Prognosis and Consultation Epidemiology Research Group who have given us permission to utilise the Code Lists (©2014).

Data sharing statement

We used anonymised data on individual patients on which the analysis, results, and conclusions reported in the paper are based. The CPRD data is not distributable under licence. However, the relevant data can be obtained directly from the agency (<https://www.cprd.com/>). The codes developed for the analysis can be available upon a valid request.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.joca.2020.03.004>.

Appendix 1

Read codes for Osteoarthritis

| Read Code | Name of the condition |
|-----------|---|
| N05zJ00 | Osteoarthritis NOS, of hip |
| N053512 | Hip osteoarthritis NOS |
| N05z511 | Hip osteoarthritis NOS |
| N053500 | Localised osteoarthritis, unspecified, pelvic region/thigh |
| N051500 | Localised, primary osteoarthritis of the pelvic region/thigh |
| N052500 | Localised, secondary osteoarthritis of pelvic region/thigh |
| N054500 | Oligoarticular osteoarthritis, unspecified, of pelvis/thigh |
| N05z500 | Osteoarthritis NOS, pelvic region/thigh |
| Nyu2E11 | [X] Unilateral secondary coxarthrosis |
| Nyu2200 | [X] Other dysplastic coxarthrosis |
| Nyu2300 | [X] Other post-traumatic coxarthrosis |
| Nyu2100 | [X] Other primary coxarthrosis |
| Nyu2E00 | [X] Other secondary coxarthrosis |
| Nyu2400 | [X] Other secondary coxarthrosis, bilateral |
| N051900 | Primary coxarthrosis, bilateral |
| N05zL00 | Osteoarthritis NOS, of knee |
| N05z611 | Knee osteoarthritis NOS |
| N053600 | Localised osteoarthritis, unspecified, of the lower leg |
| N05z600 | Osteoarthritis NOS, of the lower leg |
| N051600 | Localised, primary osteoarthritis of the lower leg |
| N052600 | Localised, secondary osteoarthritis of the lower leg |
| N054600 | Oligoarticular osteoarthritis, unspecified, of lower leg |
| N053611 | Patellofemoral osteoarthritis |
| N05zM00 | Osteoarthritis NOS, of tibio-fibular joint |
| Nyu2511 | [X] Unilateral primary gonarthrosis |
| N051B00 | Primary gonarthrosis, bilateral |
| Nyu2811 | [X] Unilateral secondary gonarthrosis |
| Nyu2800 | [X] Other secondary gonarthrosis |
| Nyu2700 | [X] Other secondary gonarthrosis, bilateral |
| Nyu2500 | [X] Other primary gonarthrosis |
| N052C00 | Post-traumatic gonarthrosis, unilateral |
| N05zN00 | Osteoarthritis NOS, of ankle |
| N05z700 | Osteoarthritis NOS, of ankle and foot |
| N05zU00 | Osteoarthritis NOS, of IP joint of toe |
| N05zT00 | Osteoarthritis NOS, of lesser MTP joint |
| N05zS00 | Osteoarthritis NOS, of 1st MTP joint |
| N05zR00 | Osteoarthritis NOS, of other tarsal joint |
| N05zP00 | Osteoarthritis NOS, of subtalar joint |
| N05z712 | Foot Osteoarthritis NOS |
| N05zQ00 | Osteoarthritis NOS, of talonavicular joint |
| N053700 | Localised osteoarthritis, unspecified, of the ankle and foot |
| N051700 | Localised, primary osteoarthritis of the ankle and foot |
| N051E00 | Localised, primary osteoarthritis of toe |
| N052700 | Localised, secondary osteoarthritis of the ankle and foot |
| N05z713 | Toe osteoarthritis NOS |
| N05z711 | Ankle osteoarthritis NOS |
| N054700 | Oligoarticular osteoarthritis, unspecified, of ankle/foot |
| Nyu2900 | [X] Other primary arthrosis of first carpometacarpal joint |
| N051C00 | Primary arthrosis of first carpometacarpal joints, bilateral |
| Nyu2A00 | [X] Other post-traumatic arthrosis/1st carpometacarpal joint |
| Nyu2B00 | [X] Other 2ndry arthrosis/1st carpometacarpal joints, bilater |
| N053400 | Localised osteoarthritis, unspecified, of the hand |
| N051400 | Localised, primary osteoarthritis of the hand |
| N05011 | Heberden's node |
| N052400 | Localised, secondary osteoarthritis of the hand |
| N05z412 | Thumb osteoarthritis NOS |
| N050700 | Heberden's node with arthropathy |
| N054400 | Oligoarticular osteoarthritis, unspecified, of hand |
| N050112 | Bouchard's node |
| N05zH00 | Osteoarthritis NOS, of DIP joint of finger |
| N050300 | Bouchard's node with arthropathy |
| N05zG00 | Osteoarthritis NOS, of PIP joint of finger |
| N05z311 | Wrist osteoarthritis NOS |
| N05z400 | Osteoarthritis NOS, of the hand |

(continued on next page)

(continued)

| Read Code | Name of the condition |
|-----------|--|
| N051D00 | Localised, primary osteoarthritis of the wrist |
| N05z411 | Finger osteoarthritis NOS |
| N05zE00 | Osteoarthritis NOS, of wrist |
| N05zF00 | Osteoarthritis NOS, of MCP joint |
| N050100 | Generalized OA of hand |
| N06z311 | Wrist arthritis NOS |
| N051800 | Localised, primary osteoarthritis of other specified site |
| N051.00 | Localised, primary osteoarthritis |
| N051z00 | Localised, primary osteoarthritis NOS |
| N051000 | Localised, primary osteoarthritis of unspecified site |
| N052.00 | Localised, secondary osteoarthritis |
| N052z00 | Localised, secondary osteoarthritis NOS |
| N052800 | Localised, secondary osteoarthritis of other specified site |
| N050000 | Osteoarthritis and allied disorders |
| N054.00 | Oligoarticular osteoarthritis, unspecified |
| N054900 | Oligoarticular osteoarthritis, unspecified, multiple sites |
| Nyu2.00 | [X]Arthrosis |
| Nyu2000 | [X]Other polyarthrosis |
| N054000 | Oligoarticular osteoarthritis, unspec, of unspecified sites |
| N05z000 | Osteoarthritis NOS, of unspecified site |
| N05.00 | Osteoarthritis and allied disorders |
| N054800 | Oligoarticular osteoarthritis, unspecified, other spec sites |
| N05z.00 | Osteoarthritis NOS |
| N053z00 | Localised osteoarthritis, unspecified, NOS |
| N053800 | Localised osteoarthritis, unspecified, of other spec site |
| N05zz00 | Osteoarthritis NOS |
| N053000 | Localised osteoarthritis, unspecified, of unspecified site |
| N05.11 | Osteoarthritis |
| N05z800 | Osteoarthritis NOS, other specified site |
| N054z00 | Osteoarthritis of more than one site, unspecified, NOS |
| N06z.11 | Arthritis |
| N050500 | Secondary multiple arthrosis |
| N050400 | Primary generalized osteoarthritis |
| N050200 | Generalized OA NOS |
| N050200 | Generalised OA Multiple sites |
| N050.00 | Generalised OA |

NOS- 'not otherwise specified.

We did not include acromio-clavicular and sterno-clavicular joint OA because of the possible accuracy of diagnosis at these joints and the expected incidence is very low.



References

- Symmons D, Mathers C, Pflieger B. Global Burden of Osteoarthritis in the Year 2000 2003, https://www3.who.int/whosis/menu.cfm?path=evidence,burden,burden_gbd2000docs&language=english.
- James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392(10159):1789–858, [https://doi.org/10.1016/S0140-6736\(18\)32279-7](https://doi.org/10.1016/S0140-6736(18)32279-7).
- Woolf AD, Pflieger B. Burden of major musculoskeletal conditions. *Bull World Health Organ* 2003;81(9):646–56.
- Rahman MM, Cibere J, Goldsmith CH, Anis AH, Kopec JA. Osteoarthritis incidence and trends in administrative health records from British Columbia, Canada. *J Rheumatol* 2014;41(6):1147–54, <https://doi.org/10.3899/jrheum.131011>.
- Yu D, Jordan KP, Bedson J, Englund M, Blyth F, Turkiewicz A, et al. Population trends in the incidence and initial management of osteoarthritis: age-period-cohort analysis of the Clinical Practice Research datalink, 1992–2013. *Rheumatology* 2017;56(11):1902–17, <https://doi.org/10.1093/rheumatology/kex270>.
- Kiadaliri AA, Rinaldi G, Lohmander LS, Petersson IF, Englund M. Temporal trend and regional disparity in osteoarthritis hospitalisations in Sweden 1998–2015. *Scand J Publ Health March* 2018, <https://doi.org/10.1177/1403494818766785>.
- Osteoarthritis In General Practice; Data and Perspectives July 2013.
- Prieto-Alhambra D, Judge A, Javaid MK, Cooper C, Diez-Perez A, Arden NK. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. *Ann Rheum Dis* 2014;73(9):1659–64, <https://doi.org/10.1136/annrheumdis-2013-203355>.
- Jordan KP, Jöud A, Bergknut C, Croft P, Edwards JJ, Peat G, et al. International comparisons of the consultation prevalence of musculoskeletal conditions using population-based healthcare data from England and Sweden. *Ann Rheum Dis* 2014;73(1):212–8, <https://doi.org/10.1136/annrheumdis-2012-202634>.
- Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, van Staa T, et al. Data Resource Profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol* 2015;44:827–36, <https://doi.org/10.1093/ije/dyv098>.
- Khan NF, Harrison SE, Rose PW. Validity of diagnostic coding within the general practice research database: a systematic review, *Br J Gen Pract* 2010;60(572):e128–36, <https://doi.org/10.3399/bjgp.10X483562>.
- Booth N. What are the Read Codes? *Health Libr Rev* (II) 1994;177–82.
- Ferguson RJ, Prieto-Alhambra D, Walker C, Yu D, Valderas JM, Judge A, et al. Validation of hip osteoarthritis diagnosis recording in the UK clinical practice research datalink. *Pharmacoepidemiol Drug Saf* October 2018, <https://doi.org/10.1002/pds.4673>.
- Kuo C-F, Grainge MJ, Mallen C, Zhang W, Doherty M. Rising burden of gout in the UK but continuing suboptimal management: a nationwide population study. *Ann Rheum Dis* January 2014, <https://doi.org/10.1136/annrheumdis-2013-204463>.
- QGIS Geographic Information System. Open Source Geospatial Foundation Project. QGIS Development Team, 2016, <http://qgis.osgeo.org>.
- Kim H-J, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med* 2000;19(3):335–51, [https://doi.org/10.1002/\(SICI\)1097-0258\(20000215\)19:3<335::AID-SIM336>3.0.CO;2-Z](https://doi.org/10.1002/(SICI)1097-0258(20000215)19:3<335::AID-SIM336>3.0.CO;2-Z).
- Joinpoint Regression Program. US: Statistical Methodology and Applications Branch, Surveillance Research Program. National Cancer Institute., 2018, <https://surveillance.cancer.gov/joinpoint/>.
- Clegg LX, Hankey BF, Tiwari R, Feuer EJ, Edwards BK. Estimating average annual percent change in trend analysis. *Statistics in Medicine* 2009;28(29):3670–8.
- Keyes KM, Utz RL, Robinson W, Li G. What is a cohort effect? Comparison of three statistical methods for modeling cohort effects in obesity prevalence in the United States, 1971–2006. *Soc Sci Med* 2010;70(7):1100–8, <https://doi.org/10.1016/j.socscimed.2009.12.018>.
- Carstensen B, Plummer M, Laara E, Hills M. Epi package for epidemiological analysis in R. Published May 23, 2019, <http://bendixcarstensen.com/Epi/>. Accessed June 11, 2019.
- Carstensen B. Demography and epidemiology: age-Period-Cohort models in the computer age, www.pubhealth.ku.dk/∼bxc 2005. Accessed January 6, 2019.

22. Nielsen B. Apc: an R package for age-period-cohort analysis. *R J* 2015;7(2), <https://journal.r-project.org/archive/2015/RJ-2015-020/RJ-2015-020.pdf>.
23. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Development Core Team, 2008, <https://www.r-project.org/>. Accessed February 13, 2019.
24. StataCorp. *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP; 2011.
25. Yu D, Peat G, Bedson J, Jordan KP. Annual consultation incidence of osteoarthritis estimated from population-based health care data in England. *Rheumatol Oxf Engl* 2015;54(11): 2051–60, <https://doi.org/10.1093/rheumatology/kev231>.
26. Brennan-Olsen SL, Cook S, Leech MT, Bowe SJ, Kowal P, Naidoo N, et al. Prevalence of arthritis according to age, sex and socioeconomic status in six low and middle income countries: analysis of data from the World Health Organization study on global AGEing and adult health (SAGE) Wave 1. *BMC Musculoskelet Disord* 2017;18:271, <https://doi.org/10.1186/s12891-017-1624-z>.
27. Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National Health and Nutrition Examination Survey 1991–94. *J Rheumatol* 2006;33:2271–9.
28. Musculoskeletal diseases profiles: November 2017 2017, <https://www.gov.uk/government/statistics/musculoskeletal-diseases-profiles-november-2017>.
29. Parsons S, Ingram M, Clarke-Cornwell AM, Symmons DPM. A HEAVY BURDEN: The occurrence and impact of musculoskeletal conditions in the United Kingdom today 2011.
30. Jordan K, Clarke AM, Symmons DPM, Fleming D, Porcheret M, Kadam UT, et al. Measuring disease prevalence: a comparison of musculoskeletal disease using four general practice consultation databases. *Br J Gen Pract J R Coll Gen Pract* 2007;57:7–14.
31. Jordan K, Porcheret M, Kadam UT, Croft P. The use of general practice consultation databases in rheumatology research (editorial). *Rheumatology* 2006;45(2):126–8.
32. Litwic A, Edwards MH, Dennison EM, Cooper C. Epidemiology and burden of osteoarthritis. *Br Med Bull* January 2013, <https://doi.org/10.1093/bmb/lds038>. lds038.
33. Doherty M. Risk factors for progression of knee osteoarthritis. *Lancet* 2001;358(9284):775–6, [https://doi.org/10.1016/S0140-6736\(01\)06006-8](https://doi.org/10.1016/S0140-6736(01)06006-8).
34. Spector TD, Campion GD. Generalised osteoarthritis: a hormonally mediated disease. *Ann Rheum Dis* 1989;48(6):523–7.
35. Nguyen U-SDT, Zhang Y, Zhu Y, Niu J, Zhang B, Felson DT. Increasing prevalence of knee pain and symptomatic knee osteoarthritis: survey and cohort data. *Ann Intern Med* 2011;155(11):725, <https://doi.org/10.7326/0003-4819-155-11-201112060-00004>.
36. Long-term trends in UK employment: 1861 to 2018 - office for national statistics. <https://www.ons.gov.uk/economy/nationalaccounts/uksectoraccounts/compendium/economicreview/april2019/longtermtrendsinukemployment1861to2018>. Accessed July 10, 2019.
37. Statistics on Obesity, Physical Activity and Diet, England 2018 April 2018, <https://files.digital.nhs.uk/publication/0/0/obes-phys-acti-diet-eng-2018-rep.pdf>.
38. Hunter DJ, Guermazi A, Roemer F, Zhang Y, Neogi T. Structural correlates of pain in joints with osteoarthritis. *Osteoarth Cart* 2013;21(9):1170–8, <https://doi.org/10.1016/j.joca.2013.05.017>.
39. Osteoarthritis - NICE CKS. <https://cks.nice.org.uk/osteoarthritis#!topicsummary>. Accessed October 21, 2018.